### **BRUCELLOSIS**

(Also known as Bang's Disease, Undulant Fever Malta Fever, and Mediterranean Fever)

# **✓ DISEASE AND EPIDEMIOLOGY**

### **Clinical Description:**

Brucellosis is a systemic disease with acute or insidious onset characterized by sustained, intermittent, or irregular fever of variable duration. Symptoms include headache, weakness, chills, profuse sweating, joint aches, depression, weight loss, and generalized aching. Localized and chronic localized infections of organs (including the liver and spleen) can occur. Complications affecting the bones and joints are common (they occur in 20–60% of cases). Involvement of the genitourinary system, including orchitis and epididymitis, (inflammation of the testes and epididymis), occurs in up to 20% of cases in males. Neurologic symptoms can occur in up to 5% of cases. The disease may last for days, months, or occasionally longer, if inadequately treated. Most cases recover, but some individuals develop significant disabilities. Relapses, involving part of or all of the original syndrome, are not uncommon. Asymptomatic infections can occur.

### **Causative Agent:**

Brucellosis is caused by bacteria of the genus *Brucella*. The species of *Brucella* that may infect humans are *B. abortus*, *B. melitensis*, *B. suis*, and rarely, *B. canis*.

# **Differential Diagnosis:**

Symptoms are non-specific and diagnosis can be delayed. This disease can be mistaken for other chronic febrile illnesses. Also culture is slow and sensitivity of culture may be low.

# **Laboratory identification:**

Clinicians can send cultures for brucella to most large reference labs. Appropriate specimens include blood (best), CSF, bone marrow, spleen, liver, body fluids and abscess aspirates. Be sure to indicate on the test request slip that brucella is suspected, as different media and/or incubation times will be used. Brucella can also be diagnosed through acute and convalescent serologies.

**Utah Public Health Laboratory (UPHL):** The UPHL will provide confirmation of clinical isolates.

#### **Treatment:**

A combination of rifampin (600-900 mg daily) or streptomycin (1 gram daily), and doxycycline (200 mg daily) for at least 6 weeks is the treatment of choice. Trimethoprim-sulfamethoxazole is effective, but relapses are common.

### Case fatality:

The case-fatality rate of untreated brucellosis is <2%; however, death may result from endocarditis caused by *B. melitensis*.

### Reservoir:

Cattle, swine, goats, and sheep are the most common reservoirs. However, brucellosis eradication programs have greatly reduced the prevalence of the disease in livestock in the U.S. Brucellosis was last identified in cattle in Massachusetts in the mid-1980s. Bison, elk, caribou, and some species of deer may also harbor *Brucella* sp. *B. canis* is an occasional problem in laboratory dog colonies and kennels; a small percentage of pet dogs and a higher proportion of stray dogs have *B. canis* antibody titers, and coyotes have been found to be infected as well.

### **Transmission:**

Brucellosis is spread to humans by direct contact with living or dead infected animals and their carcasses or secretions (including their tissues, blood, urine, vaginal discharges, aborted fetuses, and especially, placentas) Infection is transmitted by inoculation through non-intact skin or through direct contact with mucosal surfaces. It may also be spread through ingestion of raw milk and dairy products (e.g., unpasteurized cheese) from infected animals. Airborne transmission may occur through inhalation of contaminated aerosols (e.g., in laboratory settings). Persons may also be infected through accidental inoculation with live vaccine-strain *Brucella* used for livestock. Person-to-person spread is extremely rare, although it has been reported to occur through bone marrow transplantation.

## Susceptibility:

The duration of acquired immunity is uncertain.

## Incubation period:

The incubation period for brucellosis is highly variable, ranging from 5–60 days; illness most commonly occurs about 1 month after exposure.

# Period of communicability:

Person-to-person transmission of brucellosis is extremely rare.

# **Epidemiology:**

There is worldwide distribution of brucellosis. It is more common in farmers, ranchers, veterinarians, and other people who work directly with animals. It can also be found in people who work in laboratories and slaughterhouses, or as meat inspectors. Sporadic cases and outbreaks may occur among consumers of raw (unpasteurized) milk and milk products, especially soft cheeses. Less than 10% of reported cases occur in children under 19 years of age. Fewer than 120 cases per year are reported in the U.S. Most cases worldwide may be

unrecognized and under reported. Confirmed Brucella cases are rare in Utah; the last reported one was in 2004.

# **✓ PUBLIC HEALTH CONTROL MEASURES**

# Public health responsibility:

- Identify the source of infection and prevent further transmission.
- Rule out the possibility of bioterrorism; brucella is a category B agent.
- Check laboratory workers to assure that there was no exposure to the isolate, or that exposed laboratory personnel are appropriately treated.
- Notify the Department of Food and Agriculture if case was acquired in Utah.

### **Prevention:**

- Do not consume raw milk or milk products (including imported cheese).
- Workers at occupational risk (e.g., farmers, slaughterhouse workers, meat processors, or butchers) should know the symptoms of the disease, the modes of transmission, and the risks of handling infected animal carcasses and products. They should know the proper way to reduce exposure, such as ventilating slaughterhouses and handling carcasses carefully.
- Hunters should use barrier protection (e.g., gloves or clothing) when dressing wild pigs and burying the remains.
- Anyone who handles or disposes of placentas, fetuses, and/or discharges from an animal should use care and should disinfect contaminated areas.
- Local officials and farmers should search for infection among livestock and should eliminate infected animals. In areas of high prevalence, immunization of livestock may be appropriate. Ultimate control of human brucellosis relies on eliminating the disease in domestic animal populations.

## Chemoprophylaxis:

None. Exposed laboratory workers should be seen by an infectious disease physician for appropriate antibiotic treatment.

### Vaccine:

None.

# Isolation and quarantine requirements:

Isolation: None

Hospital: Body substance precautions.

Quarantine: None

# **✓ CASE INVESTIGATION**

### Reporting:

Report any illness to public health authorities that meets any of the following criteria:

- 1. A person with one or more of the following laboratory findings:
  - a. Culture and identification of *Brucella* spp. from clinical specimens
  - b. Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart
- 2. A person with fever and one or more of the clinical findings listed in Table VI-B; AND the following laboratory finding:
  - a. *Brucella* total antibody titer of greater than or equal to 160 by standard tube agglutination test (SAT) or *Brucella* microagglutination test (BMAT) in one or more serum specimens obtained after onset of symptoms
  - b. Detection of Brucella DNA in a clinical specimen by PCR assay
- A person with fever and two or more of the clinical findings listed in Table VI-B AND one or more of the epidemiological risk factors listed in Table VI-B
- 4. A person whose healthcare record contains a diagnosis of brucellosis
- 5. A person whose death certificate lists brucellosis as a cause of death or a significant condition contributing to death

Other recommended reporting procedures

- All cases of brucellosis should be reported.
- Reporting should be on-going and routine.
- Timeliness of reporting should follow the state health department's routine schedule.

Table of criteria to determine whether a brucella case should be reported to public health authorities

Criterion	1	2	3	4/5
Clinical Presentation				
Fever		N	N	
Night sweats		0	0	
Arthralgia		0	0	
Headache		0	0	
Fatigue		0	0	
Anorexia		0	0	
Myalgia		0	0	
Weight loss		0	0	

Endocarditis		0	0	
Orchitis		0	0	
Epididymitis		0	0	
Hepatomegaly		0	Ō	
Splenomegaly		0	0	
Arthritis		0	0	
Meningitis		0	0	
Spondylitis		0	0	
Healthcare record contains a diagnosis of brucellosis				0
Death certificate lists brucellosis as a cause of death or a				0
significant condition contributing to death				U
Laboratory Findings				
Culture and identification of Brucella spp. from clinical	0			
specimens	U			
Evidence of a fourfold or greater rise in Brucella antibody				
titer between acute- and convalescent-phase serum	0			
specimens obtained greater than or equal to 2 weeks apart				
Brucella total antibody titer of greater than or equal to 160				
by standard tube agglutination test (SAT) or Brucella		0		
microagglutination test (BMAT) in one or more serum		_		
specimens obtained after onset of symptoms				
Detection of Brucella DNA in a clinical specimen by PCR		0		
assay				
Epidemiological Risk Factors			Ī	I
Epidemiologically linked to a confirmed human or animal brucellosis case			0	
working in a clinical or microbiological laboratory processing samples that could potentially contain <i>Brucella</i>			0	
consumption of unpasteurized dairy products or				
undercooked meat contaminated with <i>Brucella</i>			0	
Involvement with slaughtering, dressing, or butchering of			_	
potentially infected animals			0	
Direct or indirect exposure to an environment or food			0	
products that were linked to a confirmed case of brucellosis			_	
Travel to a Brucella-endemic country			0	

#### Notes:

N = This criterion in conjunction with all other "N" and any "O" criteria in the same column is required to report or confirm a case. A number following an "N" indicates that this criterion is only required for a specific clinical presentation

O = At least one of these "O" criteria in each category (i.e., clinical presentation and laboratory findings)—in conjunction with all other "N" criteria in the same column—is required to report or confirm a case. A number following an "O" indicates that this criterion is only required for a specific clinical presentation.

# Case Definition: Brucella (2010)

### **Clinical Criteria**

An illness characterized by acute or insidious onset of fever and one or more of the following: night sweats, arthralgia, headache, fatigue, anorexia, myalgia, weight loss, arthritis/spondylitis, meningitis, or focal organ involvement (endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly).

# Laboratory Criteria for Diagnosis Definitive

- Culture and identification of *Brucella* spp. from clinical specimens
- Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart

### **Presumptive**

- Brucella total antibody titer of greater than or equal to 160 by standard tube agglutination test
- (SAT) or Brucella microagglutination test (BMAT) in one or more serum specimens obtained
- Detection of Brucella DNA in a clinical specimen by PCR assay

### **Case Classification**

### Confirmed

A clinically compatible illness with definitive laboratory evidence of *Brucella* infection

#### **Probable**

A clinically compatible illness with at least one of the following:

- Epidemiologically linked to a confirmed human or animal brucellosis case
- Presumptive laboratory evidence, but without definitive laboratory evidence, of *Brucella* infection

#### Classification Table

Criteria for defining a case of brucella.

Criterion	Confirmed	Probable	
Clinical Presentation			
Fever	N	N	N
Night sweats	0	0	0
Arthralgia	0	0	0
Headache	0	0	0
Fatigue	0	0	0
Anorexia	0	0	0
Myalgia	0	0	0
Weight loss	0	0	0
Endocarditis	0	0	0
Orchitis	0	0	0
Epididymitis	0	0	0
Hepatomegaly	0	0	0

Splenomegaly	0	0	0	
Arthritis	0	0	0	
Meningitis	0	0	0	
Spondylitis	0	0	0	
Laboratory Findings				
Culture and identification of Brucella spp. from clinical specimens	0			
Evidence of a fourfold or greater rise in Brucella antibody titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart	0			
Brucella total antibody titer of greater than or equal to 160 by standard tube agglutination test (SAT) or Brucella microagglutination test (BMAT) in one or more serum specimens obtained after onset of symptoms			0	
Detection of Brucella DNA in a clinical specimen by PCR assay			0	
Epidemiological Risk Factors				
Epidemiologically linked to a confirmed human or animal brucellosis case		0		

#### Notes:

N = All "N" criteria in the same column—in conjunction with at least one of any "O" criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—are required to classify a case.

O = At least one of these "O" (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case.

# **Case Investigation Process:**

- Fill out morbidity form
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.
- The sample must be confirmed by USL:PH or the CDC in order to confirm the case.

### **Outbreaks:**

An outbreak will constitute one case of disease without a consistent travel history to indicate infection was obtained in an endemic area such as Central/South America.

### Identification of case contacts:

This disease is not spread person-to-person. However, laboratory workers may become exposed during the culture and identification process. Public health should contact the testing laboratory(s) to see whether any personnel were exposed.

### **Case contact management:**

All exposed laboratory workers should be referred to an infectious disease physician for appropriate antibiotic management.

# **✓** REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.

Control of Communicable Diseases Manual (18<sup>th</sup> Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26<sup>th</sup> Edition), Larry K. Pickering MD, Ed; 2003.

Principles and Practice of Infectious Disease (6<sup>th</sup> Edition), Gerald L. Mandell, John E. Bennett, and Raphael Dolin Eds; 2005.

Massachusetts Department of Public Health, Guide to Surveillance, Reporting and Control, 2006.

Centers for Disease Control, Guideline for Isolation Precautions in Hospitals, 1996.

Council for State and Territorial Epidemiologists (CSTE) Position statements. Available from URL: http://www.cste.org/default.asp?page=PositionStatements